

AMENDMENTS

Amendments to the Claims

Please amend claims 24, 27, 36, 40, 44 and 48-51, as follows.

Claims 1-23. Cancelled.

24. (currently amended) A process for the isolation and purification of HMG-CoA reductase inhibitors from mycelium biomass which comprises:

clarifying a mycelium broth and concentrating the clarified broth to a lower volume,

acidifying the concentrate to a pH value in the range of 4.5 to 7.5, followed by extracting the HMG-CoA reductase inhibitor with ethyl acetate;

optionally performing lactonization;

crystallizing the HMG-CoA reductase inhibitor from:

i) a water-miscible or water-soluble first organic solvent; and

ii) a second organic solvent having limited miscibility or solubility with water at 20 °C up to 26 percent by weight.

25. (previously presented) The process according to claim 24, further comprising, before clarifying the mycelium biomass broth:

dissolving the HMG-CoA reductase inhibitor from a mycelium biomass at a pH value between 9.5 and 13 into fermentation liquor, and
adjusting the broth to a pH value between 7.5 and 8.5.

26. (previously presented) The process according to claim 25, wherein the dissolving step is carried out at a temperature in the range of 10 to 40°C for less than one hour.

27. (currently amended) The process according to claim 24, wherein clarifying the mycelium broth[er] is carried out by removing the mycelium from the broth by means of filtration.

28. (previously presented) The process according to claim 24, wherein said clarified broth is concentrated by means of reverse osmosis.

29. (previously presented) The process according to claim 24, wherein the concentrate is acidified to a pH value in the range of 5.6 to 7.5.

30. (previously presented) The process according to claim 24, wherein the concentrate is acidified to a pH value in the range of 6.0 to 7.0.

31. (previously presented) The process according to claim 24, wherein the HMG-CoA reductase inhibitor which is extracted from ethyl acetate and optionally lactonized is subjected to a purification step by adsorption chromatography.

32. (previously presented) The process according to claim 31, wherein a mixture of acetonitrile and water is used as the mobile phase for adsorption chromatography.

33. (previously presented) The process according to claim 24, wherein the order of the crystallization steps is reversed.

34. (previously presented) The process according to claim 24, wherein the water-miscible or water-soluble first organic solvent used in the crystallization step is acetone or a low alkyl alcohol.

35. (previously presented) The process according to claim 24, wherein the crystallization step from a water-miscible or water soluble first organic solvent comprises dissolving the HMG-CoA reductase inhibitor in acetone, and then adding water thereto.

36. (currently amended) The process according to claim 24, wherein the crystallization step from a second organic solvent [~~having limited miscibility or solubility with water~~] comprises dissolving the HMG-CoA reductase inhibitor in said organic solvent at a concentration of 10 to 35 g/L, and removing one-third to three-fourths of said organic solvent.

37. (previously amended) The process according to claim 24, wherein the second organic solvent used in the crystallization step is ethyl acetate.

38. (previously presented) The process according to claim 24, wherein HMG-CoA reductase inhibitors are obtained having a purity higher than 99.6%.

39. (previously presented) The process according to claim 24, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin and mevastatin.

40. (currently amended) A process for the purification of HMG-CoA reductase inhibitors which comprises subjecting the HMG-CoA reductase inhibitor to combined crystallization steps, which consist of crystallization from a water-miscible or water-soluble first organic solvent and crystallization from a second organic solvent [~~having limited miscibility or solubility with water,~~] which is selected from the group consisting of n-butanol, sec-butanol, isobutanol, amyl alcohol, hexanol, 2-ethylhexanol, benzyl alcohol, cyclohexanol, trimethylcyclohexanol, methylbenzylalcohol, methylbutyl ketone, methyl isobutyl ketone, cyclohexanone, methyl ethyl ketone, diisobutyl ketone, isophorone, trimethylcyclohexanone, methyl acetate, ethyl acetate, n-propyl acetate, isopropyl acetate, t-butyl acetate, isobutyl acetate, sec-butyl acetate, amyl acetate, butyl acetate, ethylglycol acetate, butyl glycol acetate, cyclohexyl acetate, butyl glycolate, propylene carbonate, diethyl ether, diisopropyl ether, dibutyl ether, methyl *tert*-butyl ether, methylene chloride, chloroform, 1,1,1-trichloroethane, trichloroethylene, tetrachloroethylene, nitroethane, 1-nitropropane, 2-nitropropane, hexane, toluene, p-xylene, ethylbenzene, [~~acetonitrile~~] and mixtures of these solvents, as final steps to obtain HMG-CoA reductase inhibitors having a purity higher than 99.6%.

41. (previously presented) The process according to claim 40, wherein the obtained HMG-CoA reductase inhibitors have purity higher than 99.7%.

42. (previously presented) The process according to claim 40, wherein acetone or a low alkyl alcohol is used as the water-miscible or water soluble organic solvent.

43. (previously presented) The process according to claim 40, wherein the crystallization from a water-miscible or water-soluble organic solvent comprises dissolving the HMG-CoA reductase inhibitor in acetone, and then adding water thereto.

44. (currently amended) The process according to claim 40, wherein said crystallization from a second organic solvent comprises dissolving the HMG-CoA reductase inhibitor in said second organic solvent [~~having limited miscibility or solubility with water~~] at a concentration of 10 to 35 g/L, and removing one-third to three-fourths of said organic solvent.

45. (previously presented) The process according to claim 40, wherein ethyl acetate is used as the second organic solvent .

46. (previously presented) The process according to claim 40 for the isolation and/or purification of HMG-CoA reductase inhibitors, wherein the HMG-CoA reductase inhibitors having a purity higher than 99.6% are selected from the group consisting of lovastatin, pravastatin, simvastatin and mevastatin.

47. Cancelled

48. (currently amended) A process for the isolation and purification of HMG-CoA reductase inhibitors from mycelium biomass according to claim 24, wherein the second organic solvent [which comprises:

~~clarifying a mycelium broth and concentrating the clarified broth to a lower volume,~~

~~acidifying the concentrate to a pH value in the range of 4.5 to 7.5, followed by extracting the HMG-CoA reductase inhibitor with ethyl acetate;~~

~~optionally performing lactonization;~~

~~crystallizing the HMG-CoA reductase inhibitor from:~~

~~i) a water miscible or water soluble first organic solvent; and~~

~~ii) a second organic solvent having limited miscibility or solubility with water, which is selected from the group consisting of higher alkyl alcohols, higher alkyl ketones, esters, ethers, chlorinated hydrocarbons, acetonitrile and mixtures of these solvents.~~

49. (currently amended) A process for the isolation and purification of HMG-CoA reductase inhibitors from mycelium biomass which comprises:

clarifying a mycelium broth and concentrating the clarified broth to a lower volume,

acidifying the concentrate to a pH value in the range of 4.5 to 7.5, followed by extracting the HMG-CoA reductase inhibitor with ethyl acetate; optionally performing lactonization; crystallizing the HMG-CoA reductase inhibitor from:

- i) a water miscible or water soluble first organic solvent; and
- ii) a second organic solvent [~~having limited miscibility or solubility with water,~~] which is selected from the group consisting of n-butanol, sec-butanol, isobutanol, amyl alcohol, hexanol, 2-ethylhexanol, benzyl alcohol, cyclohexanol, trimethylcyclohexanol, methylbenzylalcohol, methylbutyl ketone, methyl isobutyl ketone, cyclohexanone, methyl ethyl ketone, diisobutyl ketone, isophorone, trimethylcyclohexanone, methyl acetate, ethyl acetate, n-propyl acetate, isopropyl acetate, t-butyl acetate, isobutyl acetate, sec-butyl acetate, amyl acetate, butyl acetate, ethylglycol acetate, butyl glycol acetate, cyclohexyl acetate, butyl glycolate, propylene carbonate, diethyl ether, diisopropyl ether, dibutyl ether, methyl *tert*-butyl ether, methylene chloride, chloroform, 1,1,1-trichloroethane, trichloroethylene, tetrachloroethylene, nitroethane, 1-nitropropane, 2-nitropropane, hexane, toluene, p-xylene, ethylbenzene, [acetonitrile], and mixtures of these solvents.

50. (currently amended) A process for the purification of HMG-CoA reductase inhibitors which comprises subjecting the HMG-CoA reductase inhibitor to combined crystallization steps, which consist of crystallization from a water-miscible or water soluble first organic solvent and crystallization from a second organic solvent having limited miscibility or solubility with water at 20 °C up to 26 percent by weight, which is

selected from the group consisting of higher alkyl alcohols, higher alkyl ketones, esters, ethers, chlorinated hydrocarbons, acetonitrile, and mixtures of these solvents, as final steps to obtain HMG-CoA reductase inhibitors having a purity higher than 99.6%.

51. (currently amended) A process for the purification of HMG-CoA reductase inhibitors which comprises subjecting the HMG-CoA reductase inhibitor to combined crystallization steps, which consist of crystallization from a water-miscible or water-soluble first organic solvent and crystallization from a second organic solvent [~~having limited miscibility or solubility with water,~~] which is selected from the group consisting of n-butanol, sec-butanol, isobutanol, amyl alcohol, hexanol, 2-ethylhexanol, benzyl alcohol, cyclohexanol, trimethylcyclohexanol, methylbenzylalcohol, methylbutyl ketone, methyl isobutyl ketone, cyclohexanone, methyl ethyl ketone, diisobutyl ketone, isophorone, trimethylcyclohexanone, methyl acetate, ethyl acetate, n-propyl acetate, isopropyl acetate, t-butyl acetate, isobutyl acetate, sec-butyl acetate, amyl acetate, butyl acetate, ethylglycol acetate, butyl glycol acetate, cyclohexyl acetate, butyl glycolate, propylene carbonate, diethyl ether, diisopropyl ether, dibutyl ether, methyl *tert*-butyl ether, methylene chloride, chloroform, 1,1,1-trichloroethane, trichloroethylene, tetrachloroethylene, nitroethane, 1-nitropropane, 2-nitropropane, hexane, toluene, p-xylene, ethylbenzene, ~~[acetonitrile]~~ and mixtures of these solvents, as final steps to obtain HMG-CoA reductase inhibitors having a purity higher than 99.6%.